IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#16
AKD
11/6/02

Applicant:	Karouzakis et al.	Atty Dkt: 1581/128
Serial No:	09/762,602	Examiner: Hui,S.
Date Filed:	3/21/01	Group No: 1617
Invention:	Use of Misoprostol or/and Misoprostol acid for preparing drug in order to cure sexual dysfunction in women.	Date: October 15, 2002

CERTIFICATE OF MAILING

I hereby certify that this correspondence addressed to the Commissioner for Patents, Washington, D.C. 20231 is being deposited with the United States Postal Service as first class mail on October 15, 2002.

Morton Chirnomas

Commissioner for Patents
Washington, DC 20231

DECLARATION IN SUPPORT OF APPLICANTS' RESPONSE

[37 C.F.R. SECTION 1.132]

Dear Sir:

In support of the accompanying response to the May 15, 2002 office action in the above-referenced matter, I hereby declare as follows:

1. My name is Spiros Fotinos. I am Executive Vice President of Corporate Research and Innovation at Lavipharm SA and I am familiar with the work of Drs. Karouzakis and Kanakaris described and claimed in the present patent application for treating sexual dysfunction in women. My further qualifications are listed on the

curriculum vitae which was previously submitted as Exhibit A with my Declaration dated October 23, 2001, and which is incorporated herein by reference.

2. I have reviewed the office action dated May 15, 2002, in the above matter and have considered the statement by the Examiner that it would have been obvious for one of ordinary skill in the art at the time the invention was made to apply a topical female sexual dysfunction treating composition of misoprostol with or without another vasodilator onto the vagina or clitoris. I respectfully disagree with the Examiner.

3. Drs. Karouzakis and Kanakaris have identified for the first time that misoprostol can be especially beneficial to women when applied topically. Drs. Karouzakis and Kanakaris have further identified for the first time properties of misoprostol which make it particularly useful for topical application. Misoprostol, in contrast with alprostadil and other PGE_1 analogues, has structural characteristics which impart (1) hydrophilicity, thereby facilitating its formulation in the absence of organic solvents that act as irritants, and (2) an ability to permeate through skin and mucosa to reach target tissue.

4. I have previously explained that the cited references invariably indicate a preference for PGE_1/alpostradil. However, we now submit herewith data from studies in women, conducted by Drs. Karouzakis and Kanakaris and their colleagues, showing that the pharmacological activity of topically applied misoprostol was substantially superior to PGE_1 when topically applied. (see Appendix A). In summary, on a sample of 14 women, 71% showed a positive response to a 400μg dose of topically applied Misoprostol, versus a mere 7% response to a 25% larger 500 μg dose of PGE_1. The level of response to the PGE_1 was equal to that for the placebo at 7% response.

6. I hereby declare that all statements made herein of my own knowledge and that all statements made on information and belief are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of

the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

S. Fotinos

Dated: October 11, 2002

Exhibit A

Pharmacological effects of formulations on sexual dysfunction in female subjects having varying etiologies.

History (N)	I.Misoprostol*	II. PGE_1**	III. Placebo***
Hormonal[1] (N=1)	1	0	0
Use of drugs[2] (N=4)	3	0	0
Diabetes[3] (N=2)	2	0	0
Vascular Disorders[4] (N=2)	1	0	0
Psychological problems (N=5)	3	1	1
total (N=14)	10 (71%)	1 (7%)	1 (7%)

[1] Hyperprolactinemia
[2] Cimetidine (N=2), Phenothiazines (N=2).
[3] Use of insulin & hypoglycaemic agents
[4] Hypertension/Use of β-blockers (N=1), Peripheral vascular diseases (N=1).
* 0.5 ml Gel Misoprostol 400 µg/0.5 ml.
** PGE_1 500 µg in 0.5ml K-Y® Jelly for external use.
*** K-Y® Jelly (Johnson & Johnson).

Method: On 14 women, aged 25-55 years with sexual dysfunction of different causes, the following methods were applied successively for a few days up to 3 weeks.

I. Topical application of 0.5 ml of Misoprostol Gel at 400 µg/0.5 ml to the clitoris and vagina.
II. Topical application of 0.5ml of PGE_1 at 500 µg in 0.5ml K-Y® Jelly for external use to the clitoris and vagina.
III. Topical application of 0.5 ml of K-Y Gel (J&J) as a placebo to the clitoris and vagina.

Practition r's D ck t No. 1581/128 ***PATENT***

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent application

of _____
Inventor(s)

for _____
Title of invention

OR

In re application of: Kanakaris et al.

Application No.: 09/762,602 Group Art Unit: 1617
Filed: March 21, 2001 Examiner: Hui, S.
For: USE OF MISOPROSTOL OR/AND MISOPROSTOL ACID FOR PREPARING DRUG IN ORDER TO CURE SEXUAL DYSFUNCTION IN WOMEN

Commissioner for Patents
Washington, D.C. 20231

TRANSMITTAL OF SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT BEFORE MAILING DATE OF EITHER A FINAL ACTION OR NOTICE OF ALLOWANCE (37 C.F.R. SECTION 1.97(c))

TIME OF TRANSMITTAL OF ACCOMPANYING SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

1. The Supplemental Information Disclosure Statement transmitted herewith is being filed ***after*** three months of the filing date of this national application or the date of entry of the national stage as set forth in Section 1.491 in an international application or after the mailing date of the first Office action on the merits, whichever event occurred last but ***before*** the mailing date of either:

   (a) a final action under Section 1.113 or
   (b) a notice of allowance under Section 1.311,

   whichever occurs first.

STATEMENT OR FEE

2. Accompanying this transmittal is

A. [X] a statement as specified in 37 C.F.R. Section 1.97(e).

OR